Notice of Allowability	Application No.	Applicant(s)	
	09/853,193	VAN DEN BERGHE, GRETA	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *10/31/07*.

2. ☒ The allowed claim(s) is/are *32 and 93-96*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

1. The Request for Continued Examination (RCE) filed on October 31, 2007 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

Status of the Claims

2. Claims 32 and 93-96 are pending.

Applicant's amendment filed October 31, 2007 is acknowledged, and applicants' response has been fully considered. Claim 32 has been amended, and claims 33-36, 62-65 and 87-92 have been cancelled, and new claims 93-96 have been added. Therefore, claims 32 and 93-96 are examined.

Withdrawn Claim Objections

3. The previous objection to claims 87-92, is withdrawn in view of applicants' cancellation the claims in the amendment filed October 31, 2007.

Withdrawn Claim Rejections - 35 USC § 103

4. The previous rejection of claims 32, 33 and 62-63 under 35 U.S.C. 103(a) as being unpatentable over Scott *et al.* (Stroke 30, 793-799 (1999)) in view of Brange *et al.* (U.S. Patent 5,618,913), is withdrawn in view of applicant's amendment to the claim, applicants' cancellation of the claims, and applicants' response at page 4 of the amendment filed October 31, 2007.

5. The previous rejection of claims 32, 34 and 62-63 under 35 U.S.C. 103(a) as being unpatentable over Scott *et al.* (Stroke 30, 793-799 (1999)) in view of Anderson, Jr. *et al.* (U.S. Patent 5,547,929), is withdrawn in view of applicant's amendment to the claim, applicant's cancellation of the claim, and applicants' response at pages 4-5 of the amendment filed October 31, 2007.

6. The previous rejection of claims 35, 36 and 64-65 under 35 U.S.C. 103(a) as being unpatentable over Scott *et al.* (Stroke 30, 793-799 (1999)) in view of Havelund *et al.* (U.S. Patent 5,750,497), is withdrawn in view of applicant's cancellation of the claim, and applicants' response at page 5 of the amendment filed October 31, 2007.

Examiner's Amendment

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Richard Bork on January 30, 2008.

Examiner's Amendments to the Specification:

Please add the following paragraphs at page 6, line 13 before the subtitle "DETAILED DESCRIPTION OF THE INVENTION":

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows ICU deaths in different strata of first 24h-APACHE II and TISS scores. APACHE denotes Acute Physiology and Chronic Health Evaluation. TISS denotes Therapeutic Intervention Scoring System. Filled bars represent deaths in the RIS group and hatched bars the deaths in the IIS group.

Fig. 2 shows Kaplan-Meier cumulative survival plot for in-hospital survival. The large figure displays results from all patients (P = 0.01); the small figure displays long-stay (->5 days) ICU patients only (P = 0.018). Bold lines represent the IIS group and thin lines represent the RIS group. Patients discharged from the hospital were considered survivors. P-values were obtained by log rank (Mantel-Cox) significance testing.

Examiner's Amendments to the Claims:

Claims 32 and 93-96 have been amended as follows:

32. (Currently amended) A method of treating a critically ill patient or a critically ill polyneuropathy (CIPNP)[[-]] patient having a blood glucose level of greater than 130 mg/dL, said method comprising administering to said critically ill patient or CIPNP patient a blood glucose regulator selected from the group consisting of insulin, an insulin analogue, an active derivative of insulin or an insulin analogue, ~~or~~ and a physiologically acceptable salt of said derivative in an amount effective to reduce blood glucose levels in said patient to within a range of from about 60 mg/dL to about 130 mg/dL, wherein said blood glucose regulator is administered intravenously and continuously infused to said patient as needed for at least 24 hours and the blood glucose level is maintained within a range of from about 60 mg/dL to about 130 mg/dL for 24 hours or more and wherein said treatment reduces the incidence of mortality in ~~said patient~~ critically ill patients or CIPNP patients.

93. (Currently amended) A method of treating a critically ill patient or a critically ill polyneuropathy (CIPNP)[[-]] patient having a blood glucose level of greater than 130 mg/dL, said method comprising administering to said critically ill patient or CIPNP patient a blood glucose regulator selected from the group consisting of insulin, an insulin analogue, an active derivative of insulin or an insulin analogue, ~~or~~ and a physiologically acceptable salt of said derivative in an amount effective to reduce blood glucose levels in said patient to within a range of from about 60 mg/dL to about 130 mg/dL, wherein said blood glucose regulator is administered intravenously and continuously infused to said patient as needed for at least 24 hours and the blood glucose level is maintained within a range of from about 60 mg/dL to about 130 mg/dL for 24 hours or more and wherein said treatment reduces the incidence of critical illness polyneuropathy in ~~said patient~~ critically ill patients or CIPNP patients.

94. (Currently amended) A method of treating a critically ill patient or a critically ill polyneuropathy (CIPNP)[[-]] patient having a blood glucose level of greater than 130 mg/dL, said method comprising administering to said critically ill patient or CIPNP patient a blood

glucose regulator selected from the group consisting of insulin, an insulin analogue, an active derivative of insulin or an insulin analogue, ~~or~~ and a physiologically acceptable salt of said derivative in an amount effective to reduce blood glucose levels in said patient to within a range of from about 60 mg/dL to about 130 mg/dL, wherein said blood glucose regulator is administered intravenously and continuously infused to said patient as needed for at least 24 hours and the blood glucose level is maintained within a range of from about 60 mg/dL to about 130 mg/dL for 24 hours or more and wherein said treatment reduces the incidence of sepsis in ~~said patient~~ critically ill patients or CIPNP patients.

95. (Currently amended) A method of treating a critically ill patient or a critically ill polyneuropathy (CIPNP)[[-]] patient having a blood glucose level of greater than 130 mg/dL, said method comprising administering to said critically ill patient or CIPNP patient a blood glucose regulator selected from the group consisting of insulin, an insulin analogue, an active derivative of insulin or an insulin analogue, ~~or~~ and a physiologically acceptable salt of said derivative in an amount effective to reduce blood glucose levels in said patient to within a range of from about 60 mg/dL to about 130 mg/dL, wherein said blood glucose regulator is administered intravenously and continuously infused to said patient as needed for at least 24 hours and the blood glucose level is maintained within a range of from about 60 mg/dL to about 130 mg/dL for 24 hours or more and wherein said treatment reduces the incidence of renal failure in ~~said patient~~ critically ill patients or CIPNP patients.

96. (Currently amended) A method of treating a critically ill patient or a critically ill polyneuropathy (CIPNP)[[-]] patient having a blood glucose level of greater than 130 mg/dL, said method comprising administering to said critically ill patient or CIPNP patient a blood glucose regulator selected from the group consisting of insulin, an insulin analogue, an active derivative of insulin or an insulin analogue, ~~or~~ and a physiologically acceptable salt of said derivative in an amount effective to reduce blood glucose levels in said patient to within a range of from about 60 mg/dL to about 130 mg/dL, wherein said blood glucose regulator is administered intravenously and continuously infused to said patient as needed for at least 24

hours and the blood glucose level is maintained within a range of from about 60 mg/dL to about 130 mg/dL for 24 hours or more and wherein said treatment reduces the incidence of multiple organ failure in ~~said patient~~ critically ill patients or CIPNP patients.

The following is an **Examiner's Statement of Reasons for Allowance**: The following reference appears to be the closest art to the claimed invention. Scott *et al.* (Stroke 30, 793-799 (1999)) teach the use of a 24-hour infusion of saline (for control) or a glucose potassium insulin (GKI) infusion (including 16 U of human soluble insulin, 20 mmole of KCl in 500 ml 10% dextrose) at 100 mL/h in the treatment of 53 acute stroke patients with mild or moderate hyperglycemia (plasma glucose between 7.0 and 17.0 mmole/L, corresponding to 126 and 307 mg/dL) in an explanatory, randomized, controlled trial to test safety of the treatment, where no statistically significant differences is detected between the two groups at baseline (Table 1), and the GKI group had lower mean plasma glucose levels at 8 hours (6.4 mmole/L, corresponding to 115 mg/dL), 16 hours (6.5 mmole/L, corresponding to 117 mg/dL) and 24 hours (6.9 mmole/L, corresponding to 124 mg/dL) from the time starting infusion as compared to control, and the mean plasma glucose level is 9.1 mmole/L (corresponding to 164 mg/dL) at zero time of infusion. The reference also indicates that of the patients in the GKI group, 21 (84 %) received 2400 mL infusate compared with 24 (96%) in the control group (page 795, second column), and the infusions were maintained over next 24 hrs, however, the treatment shows no difference in the mortality rate for GKI and control groups (Table 3). Thus, the reference does not teach the treatment reduces the incidence of mortality, the incidence of critical illness polyneuropathy, the incidence of sepsis, the incidence of renal failure, or the incidence of multiple organ failure in the critically ill patients or CIPNP patients. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
January 30, 2008